pharmacology of the UTi

① UTis:.

① ↑ affects females in child-bearing age.

② 60% of females will get infected in their lifetime & ¼ will have recurrance within a year.

③ utis

- upper
  - Kidney & ureters
  - pyelonephritis.
  - fever, flank pain, frequency, nausea & vomitting.
- lower
  - bladder & urethra
  - called cystitis
  - dysuria, frequency, urgency, suprapubic pain hematuria & back pain.

④

complicated	un-complicated
occurs in patients who have predisposing lesions of the urinary tract (stones, congenital abnormalities, catheters, obstructions.....).	occurs in patients who have a healthy urinary tract.

* E.coli is the most common bacteria involved, however any type of other bacteria can cause it too.

② Antibiotics for UTis :.

- cephalosporins
- Nitrofurantoin
- fosfomycin
- Trimthoprim–sulphamethoxazole (co-trimoxazole).
- Quinolones & Fluoroquinolones

* Cats need fun Queens for tea parties.

Quinolones & fluoroquinolones

① mechanism of action

inhibit microbial DNA synthesis by inhibiting bacterial gyrase enzyme which is a type 2 topoisomerase.

② their use has been reduced due to:.

①toxicity. ②development of resistance. ③new safer microlids.

③ features:.

①they're chemotheraputic agents ②cidal

③broad spectrum → pseudomonas.

④ Side effects.

- GIT irritation; photosensitivity 	- Some have been reported to be carcinogens 
- Some are not recommended in children or during pregnancy because they may interfere with cartilage development 	- Cardiac toxicity (many may be associated with prolongation of QT interval) (many were withdrawn because of this side effect) 

⑤ Classifications.

⭐ most used ones

1st generation

① Nalidixic acid :
- ↑ effective in G-ve infections.
- only in UTIs.
- good activity against: Ecoli, proteus, Shigella, Enterobacter & Klebsiella
- No effect against pseudomonas.
- little effect against g+ve bacteria.

② pipemidic acid.
③ Oxolinic acid.

2nd generation

① Ciprofloxacin ⭐ ② Ofloxacin
③ Norfloxacin ④ Enoxacin.
⑤ lomefloxcin. ⑥ Nadifloxacin.

*lemon cone

*all exhibit more activity against G+ve & G-ve bact.

3rd generation

① levofloxacin ⭐
② Sparfloxacin
③ Gatifloxacin

4th generation.

① moxifloxacin. ⭐
② prulifloxacin.
③ Gemifloxacin. 💎

3,4 generations have good activity against pseudomonas & aneorobic micro-organisms

Note:- Ciprofloxacin & levofloxacin are mainly used in complicated utis, respiratory infections, invasive external otitis, bacterial prostatis, cervicitis & bacterial diarrhoea caused by shigella, salmonella & Ecoli.

Note:- quinolones are orally effective & well absorbed but affected by food containing Ca^{+2} & iron.

⑥ mechanisms of bacterial resistance to quinolones

- some types of bacterial efflux pumps ↓ intracellular quinolones concentration.
- produce protiens that can bind to DNA gyrase by G-ve bact. protecting it from quinolones.
- mutations in DNA gyrase/tropoisomerase → ↓ in quinolone binding affinity → ↓ its effectiveness.

Nitrofurantoin

*Synthetic bactericidal orally effective antibiotic.

①Effectiveness:.

① against G+ve & G-ve Bacteria.
② E-coli.
③ In Utis (cystitis), known as "Ut antiseptic" in this case.

② moa:.

It is converted by bacterial reductases into many reactive intermediates leading to direct damaging effect of bacterial DNA, disruption of RNA and protein synthesis and also interfering with many metabolic processes in bacteria

③features:.

- Development of resistance to nitrofurantoin is rare, due to multiple sites of action (the bacteria that is sensitive to it remain sensitive forever)
- Pulmonary fibrosis is a major side effect to nitrofurantoin
- Nitrofurantoin is contraindicated in patients with G-6-PD deficiency

Fosfomycin

It is a broad-spectrum bactericidal drug

primarily used to treat lower UTI (cystitis) and occasionally is used for prostate infections

It disrupts cell wall synthesis by inhibiting phosphoenolpyruvate synthetase and thus interferes with the production of peptidoglycan

Fosfomycin has a broad spectrum of activity against both gram-positive and gram-negative organisms, including many antibiotic-resistant organisms

It is available in 3g oral powder dosage form for reconstitution

Use of fosfomycin is commonly restricted to only a single dose because of rapid microbial resistance

Side effects:.

- Metallic taste
- Stomach upset
- Dizziness
- Stuffy nose
- Back pain
- Vaginal itching or discharge